DETAILED ACTION

The Office Action is in response to the Applicant's reply filed December 19, 2011 and to the Office action mailed on September 29, 2011.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 1, 3,5-6, 8-17, 19, 23-27 over Gowan, Jr. (US 5374659 A—previously presented), Gergely et al. (US 5834019 A – previously presented), Patel et al. (US Pat No. 6569463– previously presented), Amselem et al. (US Pat No 5747061 A), Gergely et al. (5527540), McNamara et al. (6423298– previously presented) and Hagemann et al. (US Pat 5,211,957– previously presented) is not persuasive. Therefore, the rejection is maintained for reasons of record.

Response to Arguments

Applicant's arguments filed on December 19, 2011 have been considered but are not persuasive.

"Applicants submit the references cited do not disclose the use of a pharmaceutical composition having the particular ingredients or amounts thereof as claimed." The Examiner states the claims are drawn to a composition comprising loratadine, about 0.1 to about 0.6% of a thickener said thickener comprising from about 0.1 to about 0.3% weight per volume of xanthan gum and from greater than 0 up to about 3 % weight per volume of pregelatinized starch; c) from about 1 to about 3 % weight per volume of povidone; d) from about 0.01 to about 0.05 % weight per volume of disodium EDTA; and e) from greater than 0 up to about 0.1% weight per volume of

polyoxyethylene sorbitan monooleate; wherein the pharmaceutical aqueous suspension has a pH of about 3.7 to about 8.

Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, 0.13 to 0.24% xanthan gum, 1.05 to 1.60% preglatinized starch and 0.01 to 1.00% polyoxyethylene sorbitan monooleate by weight by volume of the total suspension. Preferably citric acid, or a pharmaceutically acceptable salt thereof is added to the suspension in an amount to stabilize the pH of the solution at between 3.5 and 5.0.

The secondary references teach the specific active agent, c) from about 1 to about 3 % weight per volume of povidone and d) from about 0.01 to about 0.05 % weight per volume of disodium EDTA.

The rejections are modified below in view of applicant's amended claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3,6, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gowan, Jr. (US 5374659 A—previously presented), Gergely et al. (US 5834019 A – previously presented), Patel et al. (US Pat No. 6569463– previously

presented), Amselem et al. (US Pat No 5747061 A), Gergely et al. (5527540), McNamara et al. (6423298– previously presented) and Hagemann et al. (US Pat 5,211,957– previously presented).

Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, 0.13 to 0.24% xanthan gum, 1.05 to 1.60% preglatinized starch and 0.01 to 1.00% polyoxyethylene sorbitan monooleate by weight by volume of the total suspension. Preferably citric acid, or a pharmaceutically acceptable salt thereof is added to the suspension in an amount to stabilize the pH of the solution at between 3.5 and 5.0. Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61).

The reference fails to teach the active agent- Loratadine, the nucleation inhibitor - PVP, and the amino polycarboxylic acid compound- EDTA.

Gergely et al. is solely used to show that Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there.

Patel et al. teaches "compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional, cosmeceuticals and diagnostic agents (Col 28 line 57-67)." Such pharmaceuticals include loratadine. The pharmaceutical compositions can include one or more additive such as solubilizers, i.e., additives to increase the solubility of the pharmaceutical active ingredient (col 29 lines 16-21). The "solid pharmaceutical compositions of the present invention can optionally include one or more additives, sometimes referred to as excipients. The additives can be contained in an encapsulation coat in compositions which include an encapsulation coat, or can be part of the solid carrier, such as coated to an encapsulation coat, or contained within the components forming the solid carrier. Alternatively, the additives can be contained in the pharmaceutical composition but not part of the solid carrier itself (col 28 lines 57-67)." Hence reading on the limitation uniformly dispersed nucleation inhibitor of claim 1. Preferred solubilizers for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA. The amounts of additives can be readily determined by one skilled in the art, according to the particular properties desired. Additionally, Patel et al. teaches "Spherical particles are preferred, and these may be produced through spheronization or a spherical crystallization process. Crystals or compact granules from dry compaction or extrusion processes, often available commercially, serve as good substrates (col 41 lines 5-10)."

Amselem et al. is solely used to show that suspension formulations can comprise PVP and EDTA. Exemplified is 0.3-1.5% of PVP. EDTA may be included in the suspensions of the invention in concentrations sufficient for effective antibacterial action, preferably about 0.0001 to 0.025%, based on the weight of the suspension. The amounts of polymeric compounds and surface active agents must be determined to provide stability to suspensions. Excessive amounts of polymeric compounds may hamper the antimicrobial effects of preservatives added to the suspension. The suspensions of component (A) of the invention have a particle size of about 0.1-30 microns, preferably about 1-20 microns, most preferably about 2-10 microns in mean diameter.

Gergely et al. (5527540) teaches EDTA for example 0.05 to 0.5 part by weight when applied in aqueous solution or suspension of the total active substance phase exhibits good stability.

McNamara et al. teaches EDTA is used to improve long term storage, surfactants, and suspension stabilizing agents. The reference teaches preferred particle sizes are up to 20 microns, whilst particularly preferred particle sizes are between 5 and 15 microns, best of all not exceeding 10 microns.

Hagemann et al. teaches pharmaceutically acceptable excipients including PVP are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation (col 4 lines 42-65).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Gowan, Jr. Gergely et al. '019, Patel et al., Amselem et al., Gergely et al.,

'540, McNamara et al., and Hagemann et al. The motivation to combine the teachings is because (1) Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, a suspension stabilizing effective amount of xanthan gum (hydrocolloid and thickener), pregelatinized starch (swelling agent and thickener) and polyoxyethylene sorbitan monooleate (surfactant) (see abstact). Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61); (2) Gergely et al. teaches Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there., (3) Patel et al., teaches solubilizers for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA (4) Amselem et al. is solely used to show that suspension formulations can comprise PVP and EDTA. Exemplified is 0.3-1.5% of PVP. EDTA may be included in the suspensions of the invention in concentrations sufficient for effective antibacterial

action, preferably about 0.0001 to 0.025%, based on the weight of the suspension. The amounts of polymeric compounds and surface active agents must be determined to provide stability to suspensions. Excessive amounts of polymeric compounds may hamper the antimicrobial effects of preservatives added to the suspension. (5)Gergely et al. (5527540) teaches EDTA for example 0.05 to 0.5 part by weight when applied in aqueous solution or suspension of the total active substance phase exhibits good stability. (6) McNamara et al. teaches EDTA is used to improve long term storage, surfactants, and suspension stabilizing agents. (7) Hagemann et al. teaches pharmaceutically acceptable excipients including PVP are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation (col 4 lines 42-65). A skilled artisan would have reasonable expectation of effectively stabilizing loratadine (antihistamine) a water-insoluble pharmaceutical active.

Gowan, Jr. Gergely et al. '019, Patel et al., Amselem et al., Gergely et al., '540, McNamara et al., and Hagemann et al. meet all elemental steps of the instant claims and the compositions created thereof. Since the compositions prepared by Gowan, Jr. Gergely et al. '019, Patel et al., Amselem et al., Gergely et al., '540, McNamara et al., and Hagemann et al. meets all elemental components of the instantly prepared composition, they would obviously exhibit the same properties as recited in claims 8-10. Although the reference teaches within the embodiment of the invention crystalline drug forms are envisaged, whether the drug is in crystal form or amorphous form does not

effect the composition. Hence, the various forms are rendered obvious by the teachings of the prior art.

Saeedi et al. (Prevention Of Crystal Growth In Acetaminophen Suspensions By The Use Of Polyvinyl Pyrrolidone Bovine Serum Albumin; DARU Volume 11, No 3, 2003 – previously presented) is a relevant prior art.

The arguments are not persuasive and the rejection is made **FINAL**.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

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